

of ETRAs may be a potentially useful treatment for ALI caused by pneumonia.

doi:[10.1016/j.lfs.2014.01.056](https://doi.org/10.1016/j.lfs.2014.01.056)

Endothelin controls the IL17 production from T lymphocytes

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Endothelin (ET)-1 plays pleiotropic roles under the pathological conditions including hypertension, atherosclerosis, heart failure, cancer development and so on. Also in adaptive immune system, it has been reported that ET-1 could regulate function of dendritic cells (DCs, one of antigen-presenting cells) through the ET-1/ETA/ETB autocrine/paracrine loops. To date, however, a role of ET in autoimmune disease has not been elucidated. Here, we focused on IL-17 closely related to the pathogenesis of multiple sclerosis (MS) and investigated the effect of ET receptor blockers on the production of IL-17 from T lymphocytes. Lymph node cells (LNC) from mice at 8 days post-immunization with MOG35–55 were stimulated in vitro with MOG35–55 in the presence or absence of ETR blocker (BQ123 or BQ788). An enzyme-linked immunosorbent assay revealed that the MOG35–55-induced IL-17 production was significantly inhibited by BQ123 but not BQ788. Consistent with ELISA for IL-17, the frequency of CD4+ T cells producing IL-17 was reduced by BQ123. To further elucidate the mechanism for ET-mediated IL-17 production, in vitro model of Th17 differentiation was conducted. In condition medium of naïve T cells put under the differentiating condition for 72 h, the spontaneous release of IL-17 was increased, which was insensitive to BQ123. After the 72 h-differentiation, however, the anti-CD3/CD28 antibodies-induced IL-17 production from T cells was significantly inhibited by BQ123. These results suggest that ET/ETA signaling plays a crucial role in IL-17 production from Th17 and that BQ123 might be expected as a future therapeutic drug for the MS.

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Distinct expression of endothelin-1 and endothelin converting enzyme-1 in the lungs of patients undergoing right heart bypass surgery: A preliminary study

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Objective: In recent years, several studies demonstrated that bosentan induced clinical and hemodynamic improvement in candidates for right heart bypass surgery. We hypothesized that the endothelin system may play an important role in maintaining vasoconstriction in single ventricular physiology before and after right heart bypass surgery. **Methods:** Lung biopsy samples from two patients were subjected to immunohistological analysis. The first patient was a 27-year-old female who underwent atrio-pulmonary connection for tricuspid atresia at 4 years of age. A huge thrombus was noted on an echocardiogram in the markedly enlarged right atrium. She underwent the conversion to total cavopulmonary connection. The second patient was a 3-year-old girl with asplenia syndrome. She underwent bidirectional Glenn shunt at the age of 10 months. She had bosentan and beraprost therapy for elevated pulmonary artery pressure and pulmonary vascular resistance for 33 months. She underwent total cavopulmonary connection at 3 years of age. **Results:** Patient 1: strong positive immunostaining for endothelin-1 (ET-1) was present in endothelial cells of capillary vessels in this failed Fontan patient, whereas in normal control, only very weak staining of ET-1 in endothelial cells was observed. Patient 2: there were many ET-1 positive cells in the interstitium of alveolar wall. Most, but not all, of these cells expressed endothelin converting enzyme-1. **Conclusions:** The endothelin system may have distinct roles in the pulmonary circulation in patients with single ventricular physiology. The results of this preliminary study warrant further investigations.

doi:[10.1016/j.lfs.2014.01.058](https://doi.org/10.1016/j.lfs.2014.01.058)